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## RESEARCH LETTER

**Prevalence of COVID-19 Risk Factors and Risks of Severe Acute Respiratory Disease are Markedly Higher in Patients with Symptomatic Peripheral Arterial Occlusive Disease**

Since first being detected in December 2019 in the City of Wuhan, China, a rapidly disseminating pandemic keeps the world in suspense. While observational data on coronavirus disease 2019 (COVID-19) is still limited by its low validity and remarkable differences in screening and treatment patterns, COVID-19 vaccines are currently being divided up between countries. The first vaccination programmes started with heartening short term results, and it appears likely that the global community will need to decide which populations at risk should be immunised first.

The most vulnerable cohort with highest risk of severe illness was recently described by various publications.<sup>1</sup> Males, octogenarians, patients with cardiovascular disease, diabetes, chronic liver disease, chronic renal disease, chronic pulmonary disease, malignancy, and those with obesity and smoking are at higher risk than the healthy population. Patients suffering from symptomatic peripheral arterial occlusive disease (PAOD) are known to suffer from chronic complex multimorbidity including all these risk factors.<sup>2</sup>

Until more specific knowledge and better data on COVID-19 become available, comparable diseases such as influenza and severe acute respiratory syndrome or generally acute respiratory disease may serve as proxies for the vulnerability of a certain subgroup.

There is a lack of high quality epidemiological data on the burden of the known COVID-19 risk factors and vulnerability to severe illness. This study aimed to precisely quantify the

COVID-19 related risk profile and the risk of in hospital stay with influenza, acute respiratory distress syndrome (ARDS), or acute respiratory disease of patients with symptomatic PAOD compared with the overall population in Germany.

Longitudinal data of Germany's second largest insurance fund, BARMER, was used, including the outpatient and inpatient medical care provided to approximately 13.2% of Germany's population. The BARMER cohort has been used widely for epidemiological research before.<sup>2,3</sup>

Patients older than 40 years of age with index hospital stay for symptomatic PAOD in 2017 were included in the analysis and followed up for one year after discharge. A retrospective five year period was used to identify comorbidities. A random sample of 100 000 persons older than 40 years was drawn from the whole BARMER cohort. The German standard population census of 2011 for standardisation was used. Their index was set to 30 June 2017, denoted as the "control sample" below. All persons not continuously insured throughout the five years before the index were removed.

From the Elixhauser list of comorbidities, the following items were selected as COVID-19 risk factors: hypertension, chronic pulmonary disease, diabetes, liver disease, cancer, and obesity. Additionally, coronary artery disease, smoking, and influenza vaccination were analysed. Comorbidities were extracted from primary and secondary inpatient diagnoses and outpatient diagnoses during the previous five years. Details on the data, the PAOD cohort, and respective coding have been published previously.<sup>3</sup>

Outcomes assessed during the one year follow up after index stay were in hospital stay associated with influenza, ARDS, and acute respiratory disease.

**Table 1. Proportions and rates with 95% confidence intervals (CI) of COVID-19 risk factors, influenza vaccination, and risk of influenza, acute respiratory distress syndrome, and acute respiratory disease in patients with symptomatic peripheral arterial occlusive disease (PAOD) compared with the control group (standardised for 2011 German census)**

Comorbidities, treatment, outcome	PAOD patients (n = 11 299) proportion per 100 persons (95% CI)	Control sample (n = 99 730) proportion per 100 persons (95% CI)	Risk ratio (95% CI)
Smoking	52.1 (48.5–56.0)	13.1 (12.8–13.3)	3.99 (3.92–4.06)
Diabetes	46.6 (43.7–49.7)	21.1 (20.8–21.4)	2.21 (2.15–2.28)
Coronary artery disease	41.9 (39.4–44.6)	22.8 (22.5–23.1)	1.84 (1.78–1.90)
Hypertension	83.1 (79.2–87.2)	54.7 (54.3–55.2)	1.52 (1.47–1.57)
Obesity	31.6 (29.0–34.3)	21.1 (20.8–21.4)	1.50 (1.41–1.58)
Liver disease	26.1 (24.0–28.4)	18.9 (18.6–19.1)	1.39 (1.30–1.47)
Chronic pulmonary disease	46.9 (43.8–50.1)	36.1 (35.7–36.5)	1.30 (1.23–1.37)
Cancer	22.4 (20.6–24.3)	21.2 (21.0–21.5)	1.06 (0.97–1.14)
Influenza vaccination	37.2 (35.0–39.6)	29.8 (29.4–30.1)	1.25 (1.19–1.31)
Influenza within one year, per 10 000 person years	63.6 (24.2–135.2)	13.4 (11.2–15.9)	4.75 (3.95–5.54)
Acute respiratory distress syndrome, per 10 000 person years	8.3 (3.9–15.5)	1.9 (1.1–3.0)	4.36 (3.57–5.15)
Acute respiratory disease, per 10 000 person years	734.3 (615.5–869.3)	164.1 (156.1–172.4)	4.47 (4.30–4.65)

CI = confidence interval.

Age and sex standardised rates and rate differences per 1 000 persons (risk factors) and 1 000 person years (outcomes) with 95% confidence intervals were computed.

Patients with symptomatic PAOD ( $n = 11\,299$ ) were more often males (52.8%) and older (mean age  $73.3 \pm 11.0$  years) than the control sample ( $n = 99\,730$ , 35.9% male, mean age  $63.1 \pm 12.9$  years).

Standardised for these differences, Patients with PAOD had a less favourable risk factor profile than the control sample (see Table 1). Risks were elevated for smoking, diabetes, coronary artery disease, hypertension, obesity, liver disease, and chronic pulmonary disease, but not for cancer. Influenza vaccination was noted more often in Patients with PAOD than in the control sample.

The risk of inpatient hospital stay associated with influenza, ARDS, and acute respiratory disease was more than four times higher in patients with PAOD than in the control sample. Of 10 000 persons, 63.6 suffered from influenza, 8.3 from ARDS, and 734.3 from acute respiratory disease during one year follow up after index stay.

These results confirm that patients treated for symptomatic PAOD are not only older and more often male but also face considerably elevated COVID-19 risk factors and are particularly susceptible to severe respiratory disease associated with in hospital stay. Despite a higher likelihood for influenza vaccination in patients with PAOD, rates are still considerably below national coverage goals and recommendations in the American Heart Association/American College of Cardiology guidelines.<sup>4</sup> This is particularly worrying since influenza like illnesses are not only related to higher risk of adverse respiratory events but also to cardiovascular morbidity and all cause mortality in patients with coronary and other atherosclerotic vascular disease.<sup>5</sup>

In the light of these findings, patients with symptomatic PAOD should receive high priority with respect to protective measures, polymerase chain reaction, antibody testing, and vaccination. The strikingly low influenza vaccination rates that clearly missed the European and national coverage goals emphasise the importance of awareness campaigns and future research to identify underlying causes.

#### CONFLICTS OF INTEREST

None.

#### FUNDING

The present analyses were part of the RABATT project (Funded by the German Joint Federal Committee; grant-no. 01VSF18035).

#### ACKNOWLEDGEMENTS

The authors are grateful for the support and submission of data from BARMER. The authors would like to thank Thea Kreutzburg and Jenny Kuchenbecker (both GermanVasc) for supporting the statistical analyses.

#### REFERENCES

- 1 Docherty AB, Harrison EM, Green CA, Hardwick HE, Pius R, Norman L, et al. ISARIC4C investigators. Features of 20 133 UK patients in hospital with covid-19 using the ISARIC WHO Clinical Characterisation Protocol: prospective observational cohort study. *BMJ* 2020;**369**:m1985.
- 2 Kreutzburg T, Peters F, Rieß HC, Hischke S, Marschall U, Kriston L, et al. Editor's Choice – Comorbidity patterns among patients with peripheral arterial occlusive disease in Germany: a trend analysis of health insurance claims data. *Eur J Vasc Endovasc Surg* 2020;**59**:59–66.
- 3 Behrendt CA, Sedrakyan A, Peters F, Kreutzburg T, Schermerhorn M, Bertges DJ, et al. Editor's Choice – Long term survival after femoropopliteal artery revascularisation with paclitaxel coated devices: a propensity score matched cohort analysis. *Eur J Vasc Endovasc* 2020;**59**:587–96.
- 4 Gerhard-Herman MD, Gornik HL, Barrett C, Barshes NR, Corriere MA, Drachman DE, et al. 2016 AHA/ACC Guideline on the management of patients with lower extremity peripheral artery disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation* 2017;**135**:e726–79.
- 5 Davis MM, Taubert K, Benin AL, Brown DW, Mensah GA, Baddour LM, et al. Influenza vaccination as secondary prevention for cardiovascular disease: a science advisory from the American Heart Association/American College of Cardiology. *J Am Coll Cardiol* 2006;**48**:1498–502.

**Frederik Peters**

Department of Vascular Medicine, Research Group GermanVasc, University Medical Centre Hamburg-Eppendorf, Hamburg, Germany

**Ursula Marschall**

BARMER, Wuppertal, Germany

**Christian-Alexander Behrendt\***

Department of Vascular Medicine, Research Group GermanVasc, University Medical Centre Hamburg-Eppendorf, Hamburg, Germany

\*Corresponding author: Department of Vascular Medicine, Research Group, GermanVasc, University Medical Centre Hamburg-Eppendorf, Hamburg, Germany.

Email-addresses: [behrendt@hamburg.de](mailto:behrendt@hamburg.de) (Christian-Alexander Behrendt)

 VAScevidence.

Available online 5 March 2021

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<https://doi.org/10.1016/j.ejvs.2021.02.055>